Announcement of Federal Funding Opportunity

Summary

I. GENERAL INFORMATION

A. Title of Award: Clinical Trial Development Award (CTDA).

B. Program Name: DOD FY04 Neurofibromatosis Research Program (NFRP).

C. Funding Opportunity Number: NF04-CTDA.

D. Agency Name: USAMRMC, Office of the Congressionally Directed Medical Research Programs (CDMRP), 1077 Patchel Street, Fort Detrick, Maryland 21702-5024.

E. Agency Contact(s):

1. Questions related to the Program, proposal format, or required documentation may be addressed to the CDMRP at:

Phone: 301-619-7079
Fax: 301-619-7792
E-mail: cdmrp.pa@det.amedd.army.mil
Mail: Commander
US Army Medical Research and Materiel Command
ATTN: MCMR-PLF (NF04-CTDA)
1077 Patchel Street (Building 1077)
Fort Detrick, MD 21702-5024

2. Questions related to electronic submission: The help line phone number is 301-682-5507 and is also provided on the web. Other help desk contact information is:

Website: https://cdmrp.org/proposals (the proposal submission website)
E-mail: help-proposals-cdmrp@cdmrp.org

F. Anticipated Instrument Type(s): Grants/Cooperative Agreements.

G. Catalog of Federal Domestic Assistance (CFDA) Number(s): 12.420; Military Medical Research and Development.

H. Website Address to Access Application Package: Proposals must be submitted electronically at https://cdmrp.org/proposals. The website contains all the information, forms, documents, and links you will need to apply.

I. Award/Regulatory Approval: Please note, each award mechanism has specific requirements regarding human subjects and animal use. Please see the full text of the Program Announcement for details pertaining to this award mechanism.

Once an award is made, the applicant may not use, employ, or subcontract for the use of any human subjects, human anatomical substances, or laboratory animals without express written permission from the applicable USAMRMC Regulatory Compliance and Quality (RCQ) office. USAMRMC RCQ will forward these express written approvals directly to the applicant with a copy furnished to the institution's Sponsored Programs Office (or equivalent).

II. FUNDING OPPORTUNITY DESCRIPTION

The intent of the Clinical Trial Development Award is to provide support for the development of a multi-institutional neurofibromatosis (NF)-related clinical trial, including the establishment of the research team, the development of tools for data management and trial/research administration, the definition of recruitment strategies, and the development of the clinical protocol and other essential components of the study included in a Manual of Operations and Procedures. The goal of these awards is to develop clinical trials with the potential to have a major impact on the treatment of either NF1, NF2, or Schwannomatosis.

III. AWARD INFORMATION

- Type of award: grant/cooperative agreement.
- A total of approximately $0.5 million (M) is available for this award mechanism.
- It is anticipated that approximately three proposals will be funded.
- Funding for Clinical Trial Development Awards can be requested for $150,000 for 18 months, inclusive of both direct and indirect costs. Funding will be disbursed in two installments, one installment of $100,000 at the time of the award and the second installment of $50,000 contingent upon submission of a compliant Fiscal Year 2005 (FY05) Clinical Trial Award proposal, clinical protocol, and consent form.

IV. ELIGIBILITY INFORMATION

A. Applicants: Applicants from all academic levels are eligible to submit proposals.

B. Institutions: Eligible institutions include for-profit, non-profit, public, and private organizations.

C. Cost Sharing: It is expected that institutions will cost share. Please see "Major Equipment" located in Subsection V.F.2.c of the Full Text of Program Announcement for details.

D. Other Eligibility Criteria: Please see the Full Text of Program Announcement description for details regarding duplicate submissions, applications from Historically Black Colleges and Universities/Minority Institutions, and administrative compliance issues.

V. PROPOSAL PREPARATION AND SUBMISSION INFORMATION

A. Proposal Information: Applicants are required to submit the Proposal Information prior to upload of the proposal. Complete the Proposal Information as described at https://cdmrp.org/proposals.

B. Proposal Preparation: All proposals must be converted into an electronic PDF (Portable Document Format) file for electronic proposal submission. Please see the Full Text of Program Announcement for details.

C. Submission Dates and Times: Deadline Date: May 4, 2004. Proposals must be approved on the CDMRP eReceipt system by the Contract Representative at the applicant's institutional Sponsored Programs Office (or equivalent) by 5:00 p.m. (Eastern time).

D. Electronic Submission Requirements: Electronic submission is required. No paper copy submissions will be accepted. Proposals must be submitted electronically at https://cdmrp.org/proposals. Please see the Full Text of Program Announcement for details.

VI. PROPOSAL REVIEW INFORMATION

Clinical Trial Development Award proposals will be scientifically and programmatically reviewed by the NFRP Integration Panel (IP), which is composed of scientific experts, clinicians, and consumer advocates. The IP will determine which proposals best fulfill the intent of the award mechanism.

VII. AWARD ADMINISTRATION INFORMATION

A. Award Notices and Administrative Requirements: Details of award notification procedures, and administrative requirements including Regulatory Compliance and Quality documents (Certificate of Environmental Compliance, Research Involving Human Subjects and/or Anatomical Substances, Research Involving Animals, and Safety Program Plan) can be found in the Full Text of Program Announcement.

B. Reporting Requirements: Annual reporting requirements apply.

Full Text of Program Announcement

I. GENERAL INFORMATION

A. Title of Award: Clinical Trial Development Award (CTDA).

B. Program Name: DOD FY04 Neurofibromatosis Research Program (NFRP).

C. Funding Opportunity Number: NF04-CTDA.

D. Agency Name: USAMRMC, Office of the Congressionally Directed Medical Research Programs (CDMRP), 1077 Patchel Street, Fort Detrick, Maryland 21702-5024.

E. Agency Contact(s):

1. Questions related to the Program, proposal format, or required documentation: Applicants should submit questions as early as possible. Every effort will be made to answer questions within 5 working days.

Phone:	301-619-7079
Fax:	301-619-7792
E-mail:	cdmrp.pa@det.amedd.army.mil
Mail:	Commander US Army Medical Research and Materiel Command ATTN: MCMR-PLF (NF04-CTDA) 1077 Patchel Street (Building 1077) Fort Detrick, MD 21702-5024

2. Questions related to electronic submission: Help lines will be available to answer specific questions regarding the preparation of proposals for electronic submission or the process of electronic submission. The help line phone number is 301-682-5507 and is also provided on the web. Other help desk contact information is:

Website:	https://cdmrp.org/proposals (the proposal submission website)
E-mail:	help-proposals-cdmrp@cdmrp.org

F. Anticipated Instrument Type(s): The USAMRMC implements its extramural research program predominantly through the award of grants and cooperative agreements. More information on these funding instruments may be obtained by request from:

Fax:	301-619-2937
E-mail:	qa.baa@det.amedd.army.mil
Mail:	Director US Army Medical Research Acquisition Activity ATTN: MCMR-AAA 820 Chandler Street Fort Detrick, MD 21702-5014

G. Catalog of Federal Domestic Assistance (CFDA) Number 12.420: Military Medical Research and Development.

H. Website to Access Application Package: Proposals must be submitted electronically at https://cdmrp.org/proposals. This website will contain all the information, forms, documents, and links you will need to apply. If you experience difficulties in downloading documents, contact the CDMRP as indicated in Subsection E.1 above.

I. Award/Regulatory Approval: Please note, each award mechanism has specific requirements regarding human subjects and animal use.

Once an award is made, the applicant may not use, employ, or subcontract for the use of any human subjects, human anatomical substances, or laboratory animals without express written permission from the applicable USAMRMC Regulatory Compliance and Quality (RCQ) office. USAMRMC RCQ will forward these express written approvals directly to the applicant with a copy furnished to the institution's Sponsored Programs Office (or equivalent).

II. FUNDING OPPORTUNITY DESCRIPTION

A. Program History: The Clinical Trial Development Award is part of the DOD NFRP, which was established in Fiscal Year 1996 (FY96) to promote research directed toward decreasing the impact of neurofibromatosis (NF). Appropriations for the NFRP since FY96 total $130.3 million (M). The program history of the FY96-03 NFRP is shown in Table 1. The FY04 appropriation is $20M.

Table 1: History of the DOD's Peer Reviewed NFRP

Program History	FY96-02	FY03
Congressional Appropriations for NFRP	$90.3M	$20M
Total Proposals Received	299	62
Total Proposals Funded	103	~13[1]
Clinical Trial Development Award Proposals Received	N/A	2
Clinical Trial Development Award Proposals Funded	N/A	~1[1]

[1] Award negotiations will be finalized by September 2004.

B. Program Objectives: The overall goal of the FY04 NFRP is to develop effective therapies for NF1, NF2, and Schwannomatosis. Within this context, support for the training of NF researchers, the encouragement of established scientists in the field, and the attraction of new scientific expertise from other fields are essential to the NF community. Proposals to the NFRP are sought across all areas of laboratory, clinical, behavioral, and epidemiological research including all disciplines within the basic, clinical, psychosocial, behavioral, sociocultural, and environmental sciences; nursing; occupational health; alternative therapies; public health and policy; and economics. Additionally, proposals that address the needs of minority, low-income, rural, and other under-represented and/or medically underserved populations may be submitted from any eligible institutional source. Proposals are encouraged from investigators working at Historically Black Colleges and Universities/Minority Institutions (HBCU/MI).

C. Award Mechanism Description: Due to the scope and magnitude of the NFRP Clinical Trial Awards, the Clinical Trial Development Award has been instituted to provide support for the development of a multi-institutional NF-related clinical trial, including the establishment of the research team, the development of tools for data management and trial/research administration, the definition of recruitment strategies, and the development of the clinical protocol and other essential components of the study included in a Manual of Operations and Procedures. The goal of these awards is to develop clinical trials with the potential to have a major impact on the treatment of either NF1, NF2, or Schwannomatosis. Participating institutions must be willing to resolve potential intellectual property issues and to remove institutional barriers that might interfere with achieving high levels of cooperation to ensure the successful completion of the clinical trials. An intellectual property plan agreed upon by all participating institutions is required as part of the administrative documentation of this proposal (see V.E.14).

The Clinical Trial Development Award proposal should briefly describe:

- The objective and rationale of the proposed clinical trial, including any preclinical science and preliminary clinical research relevant to the trial;
- The relevance of the proposed clinical trial to NF1, NF2, and/or Schwannomatosis;
- The proposed intervention(s) to be tested in the clinical trial, with a brief description, as appropriate, of its:
    a. Source,
    b. Investigational New Drug (IND) status,
    c. Availability of the substance in sufficient quantity under current Good Manufacturing Practice (cGMP) production,
    d. Dosing and toxicity,
    e. Mechanisms of action, and
    f. Preclinical/clinical evidence of efficacy;
- A preliminary estimate of sample size for the clinical trial, a preliminary patient accrual/recruitment schedule, and evidence of access to appropriate patient population(s);
- A plan for the development of a clinical protocol (Manual of Operations and Procedures) and consent/assent form(s) that follows the Human Subjects Research Review Board (HSRRB)-prescribed format*;
- The outline of a plan for obtaining internal scientific and local Institutional Review Board (IRB) reviews for the clinical protocol and consent/assent form(s) at the highest possible level within the participating institutions, up to and including preliminary IRB approval if available at your institution, by the time of the Clinical Trial Award proposal submission;
- The outline of a plan for addressing human subjects protection requirements as outlined by the HSRRB at https://cdmrp.org/programAnnouncements.cfm under "Regulatory Document Forms"*;
- An outline of a clinical trial management plan, including a plan for ensuring the standardization of procedures across sites and among staff; and
- Evidence of preliminary institutional commitment to the proposed clinical trial.

The Clinical Trial Development Award has been instituted to facilitate the funding of a quality clinical trial and the rapid accrual of patients into the trial through a well-developed, ***HSRRB-approved*** clinical protocol. The purpose of the Clinical Trial Development Award is not to obtain preliminary data or to conduct studies to support the rationale for the proposed clinical trial; therefore, *funds may not be used to*

support laboratory or preclinical research. However, funds from the Clinical Trial Development Award may be used to:

- Support meetings, teleconferences, and travel among participating investigators to develop the clinical trial and associated protocol and consent/assent form(s);
- Furnish salary support during clinical protocol development;
- Develop and implement a data management, real-time communications, and/or administration plan for the proposed clinical trial;
- Reimburse the Principal Investigator's (PI's) institution for costs associated with conducting the IRB review of the proposed clinical protocol and consent form;
- Provide other costs directly associated with planning and developing the clinical trial;
- Coordinate consent/assent forms and other IRB and/or HSRRB issues between different institutions for multi-institutional trials;
- Resolve intellectual property and material rights among institutions, companies, and investigators;
- Develop definitive statistical plans; and
- Develop sources and obtain letters affirming intervention supply or availability.

One requirement of the Clinical Trial Development Award will be the submission of a proposal to the NFRP Clinical Trial Award in FY05, pending receipt of funds by the NFRP. Another product of this award mechanism will be a detailed clinical protocol or "Manual of Operations and Procedures" for the proposed clinical trial. This protocol should be in the HSRRB-approved format*. The proposal, clinical protocol, and consent/assent form(s) must all be submitted as part of the application for the Clinical Trial Award in FY05. Failure to submit a Clinical Trial Award proposal in FY05 after receipt of an FY04 Clinical Trial Development Award will result in a forfeit of the second installment of the Clinical Trial Development Award funding. Selection to receive an FY04 Clinical Trial Development Award and submission of an FY05 Clinical Trial Award proposal do not guarantee an FY05 Clinical Trial Award. The FY05 Clinical Trial Award also will be open to all eligible applicants with clinical trials relevant to NF1, NF2, and/or Schwannomatosis irrespective of receipt of an FY04 Clinical Trial Development Award.

**Please note that all DOD-funded research involving human subjects and/or human anatomical substances must be reviewed and approved by the HSRRB in addition to local IRBs. It is recommended that all protocols be prepared according to the guidelines provided in the document titled "Research Involving Human Subjects and/or Anatomical Substances," which can be found at* https://cdmrp.org/programAnnouncements.cfm *under "Regulatory Document Forms." An HSRRB-approved template for the protocol also can be found at this site.*

Please note there is no guarantee that funds will be available for Clinical Trial Awards in FY05.

III. AWARD INFORMATION

Funding for the Clinical Trial Development Award in FY04 is up to $150,000 per award inclusive of both direct and indirect costs for 18 months; funds will be disbursed in two installment payments of $100,000 and $50,000 each, pending proposal, protocol, and consent form submission. Funds from both installments of the Clinical Trial Development Award can cover administrative support including salary, meetings and related travel among participating investigators, database generation and software

development, purchase of computers, design of websites, teleconferences, and other costs directly associated with planning and developing the clinical trial. Travel costs may not exceed $1,800 per year per investigator. *Funds may not be used to support laboratory research.*

Disbursement of the Clinical Trial Development Award funds will be made in two installments. The first installment of $100,000 will be made at the time of the award; the second installment of $50,000 will be made after the submission of a compliant Clinical Trial Award proposal, clinical protocol, and consent form. **Failure to submit a Clinical Trial Award in FY05 after receipt of an FY04 Clinical Trial Development Award will result in a forfeit of the second installment of the Clinical Trial Development Award funding.**

The nature of this Program does not allow for renewal of grants or supplementation of existing grants. Approximately $0.5M is available to the NFRP for the Clinical Trial Development Awards. Depending on the number and quality of the applications, it is anticipated that approximately three proposals will be funded.

IV. ELIGIBILITY INFORMATION

A. Applicants: All individuals, regardless of ethnicity, nationality, or citizenship status, may apply as long as they are employed by, or affiliated with, an eligible institution as defined below.

B. Institutions: Eligible institutions include for-profit, non-profit, public, and private organizations. Examples include universities, colleges, hospitals, laboratories, companies, and agencies of local, state, and federal governments. The USAMRMC is especially interested in receiving applications from HBCU/MI.

C. Cost Sharing: It is expected that institutions will cost share. Please see full details under "Major Equipment" located in Subsection V.F.2.c.

D. Other Eligibility Criteria:

1. Duplicate Submissions: Submission of the same research project to the FY04 NFRP under different award mechanisms or to other CDMRP programs is discouraged. The Government reserves the right to reject duplicative proposals.

2. HBCU/MI: A goal of the DOD is to allocate funds for the CDMRP's peer reviewed research to fund proposals from HBCU/MI. This provision is based upon guidance from Executive Orders.[1] Proposals submitted to the DOD are assigned HBCU/MI status if the submitting institution is so designated by the Department of Education on the date that the program announcement is released. The Department of Education list is posted on the CDMRP website under Minority Institutions at http://cdmrp.army.mil/funding/pdf/minfrp020604.pdf.

3. Administrative Compliance Issues: Compliance guidelines have been designed to ensure the presentation of all proposals in an organized and easy-to-follow manner. Peer reviewers expect to see a consistent, prescribed format for each proposal. Nonadherence to format requirements makes proposals difficult to read, may be perceived as an attempt to gain an unfair competitive advantage, and may result in proposal rejection or a lower global priority score.

[1] Executive Orders 12876, 12900, and 13021

The following will result in administrative rejection of the entire proposal prior to peer review:

- Proposal body exceeds page limit.
- Proposal body is missing.
- Detailed cost estimate is missing.
- Proposal is incomplete after the deadline.
- Required administrative documentation is not included.

For any other sections of a proposal with a defined page limit, any pages over the specified limit will be removed from the proposal and not forwarded for peer review.

Unless specifically requested by the Government, any material submitted after the submission deadline will not be forwarded for peer review.

V. PROPOSAL PREPARATION AND SUBMISSION INFORMATION

A. Proposal Components Summary: This subsection is a summary of submission requirements. Details, URLs, and other links are provided in the appropriate subsections of this program announcement.

The PI is responsible for uploading the following information:

- **Proposal Information:** The Proposal Information consists of two parts, both of which are entered as data fields. A Letter of Intent is generated when Part 1 of the Proposal Information is saved.
- **Statement of Work (SOW) and Proposal Abstracts:** The SOW, Technical Abstract, and Public Abstract are each entered as a separate data field.
- **Proposal:** The proposal is uploaded as a PDF (Portable Document Format) file under the "Required Files" tab.
- **Budget Information:** The budget information is uploaded as a PDF file under the "Required Files" tab.
- **Regulatory Documents:** The Certificate of Environmental Compliance and the Principal Investigator Safety Program Assurance form are each uploaded as separate PDF files under the "Required Files" tab.

The Contract Representative or institutional official responsible for sponsored program administration (or equivalent) from the applicant's institution is responsible for the following:

- **US Army Medical Research Acquisition Activity (USAMRAA) Documents:** The institute's currently negotiated "Rate Agreement," "Certifications and Assurances for Assistance Agreements," and the "Representations for Assistance Agreements" are to be uploaded as separate PDF files under the Contract Representative's "My Profile" tab.
- **Approval:** The Contract Representative or institutional official responsible for sponsored program administration must provide approval of all proposal components (Proposal Information, SOW, Abstracts, Proposal, Budget Information, and Regulatory documents). Contract Representative approval must occur prior to the submission deadline of 5:00 p.m.

(Eastern time) May 4, 2004. The eReceipt system will **not** accept data entry, file uploads, or approvals submitted after the 5:00 p.m. Eastern time May 4, 2004 deadline.

B. Proposal Information: Applicants are required to submit the Proposal Information, Parts 1 and 2, prior to upload of the proposal and the budget information. Complete the Proposal Information as described in https://cdmrp.org/proposals. The Proposal Information must include the e-mail address of a representative from the Sponsored Programs Office (or equivalent) who is authorized to negotiate on behalf of the institute.

- **Letter of Intent:** An electronic Letter of Intent should be submitted by April 6, 2004. To accomplish this, the applicant should complete Part 1 of the Proposal Information section at https://cdmrp.org/proposals, then save the information by clicking on the "Save and Forward Letter of Intent" button. This information may be changed at any time until the applicant submits the final Proposal Information by clicking on the "Submit Final" button.

C. SOW – 11,400-character limit, including spaces (approximately two pages): The SOW is captured as a data field under the "SOW/Abstract" tab in the CDMRP eReceipt system. To submit the SOW, the applicant may either type in the SOW or "cut and paste" it from a word processing application into the data field. Sample SOWs can be found at https://cdmrp.org/samples.cfm.

The SOW is a concise restatement of the research proposal that outlines, step by step, how each of the major goals or objectives of the proposed research/services will be accomplished during the timeline for which the USAMRMC will provide financial support.

As appropriate, the SOW should:

- Describe the work to be accomplished as tasks (tasks may relate to specific aims),
- Identify the timeline and milestones for the work over the period of the proposed effort,
- Indicate the numbers of research subjects (animal or human) and/or anatomical samples projected or required for each task,
- Identify methods, and
- Identify outcomes, products, and deliverables for each phase of the project.

D. Proposal Abstracts: Abstracts are not required for the Clinical Trial Development Award application process, but the data fields must be completed for the final submission. Therefore, the applicant should type "N/A" into both abstract data fields.

E. Proposal:

1. Format: All proposals must be converted into an electronic PDF file for electronic submission. Proposals must be uploaded under the "Required Files" tab of the CDMRP eReceipt system. Applicants unfamiliar with the preparation of PDF files are encouraged to acquire appropriate software and learn the process before the submission deadline. To prepare proposals for PDF submission, the instructions in this subsection must be followed carefully.

The proposal must be clear and legible and conform to the following guidelines:

- Type Font: 12 point, 10 pitch.
- Type Density: No more than 15 characters per inch. (For proportional spacing, the average for any representative section of text should not exceed either 15 characters per inch or 114 characters per line.)
- Spacing: Single-spaced between lines of text, no more than five lines of type within a vertical inch.
- Margins: Minimum of 0.5-inch top, bottom, right, and 1-inch left.
- Color, Resolution, and Multimedia Objects: Proposals may include color, high resolution, or multimedia objects (e.g., MPEG, WAV, or AVI files) embedded in the PDF files; however, these items must not exceed 15 seconds in length and a size of 10 megabytes (MB). Since some reviewers work from black and white printed copies, applicants may wish to include text in the proposal directing the reviewer to the electronic file for parts of the proposal that may be difficult to interpret when printed in black and white.
- Spell out all acronyms the first time they are used. One page following the proposal body is allocated to spell out acronyms, abbreviations, and symbols.
- Language: English.
- Print Area: 7.0 x 10.0 inches (approximately 18 cm x 25.5 cm).

2. Title/Referral Page: No page limit. Complete the Title/Referral Page, which can be downloaded at https://cdmrp.org/programAnnouncements.cfm?prg=NFRP&prg_fy=2004. Complete each section as described:

a. Proposal title (up to 160 characters).

b. Proposal log number (this will be automatically provided when the Proposal Information is completed and saved).

c. PI's full name (first, middle initial, last).

d. Submitting institution.

e. Award mechanism: Type in "Clinical Trial Development Award."

f. Keyword descriptive technical terms: To assist the staff in assigning proposals to the appropriate scientific peer review panel, please specify the subject area of the proposal. Also, list specific keywords and descriptive technical terms that would best describe the technical aspects of the project.

g. Conflicts of interest: To avoid real and apparent conflicts of interest during the review process, list the names of all scientific participants in the proposal including consultants, collaborators, and subawardees. In addition, list the names of other individuals outside the scope of this proposal who may have a conflict of interest in review of this proposal. Provide the following information for each participant: name, institutional affiliation(s), and, if applicable, his or her role(s) on the proposed project.

3. Table of Contents/Checklist: Start section on a new page; one-page limit. Prepare a Table of Contents/Checklist, with page numbers. Number all pages consecutively at the bottom center, beginning with the Title/Referral Page.

4. Proposal Relevance Statement: Start section on a new page; one-page limit. Applicants should state explicitly how the proposed work is relevant to NF and describe how the proposed research is pertinent to one or more critical issues of the disease.

5. Proposal Resubmission Statement (optional): Start section on a new page; two-page limit. Proposals that have been declined for funding in a previous year may be resubmitted to the NFRP. Resubmitted/revised proposals must meet all requirements for the Clinical Trial Development Award proposals described in this program announcement. Resubmitted/revised proposals should include a two-page section that addresses the issues identified in the peer review summary statement of the previously unfunded application. This section should address all aspects of the critique from the previous peer and programmatic reviews and should reference any new preliminary data included. A copy of the summary statement from the unfunded application also should be included and placed immediately after the resubmission statement.

Applicants should be aware that the year-to-year status of funding for the NFRP does not permit establishment of standing panels for scientific peer review. Therefore, the submission of a revised proposal does not guarantee funding or an improved global priority score.

6. Main Body: Start section on a new page; six-page limit inclusive of any figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, and other relevant information needed to judge the proposal. It is the responsibility of the investigator to clearly articulate how the proposed plan for a clinical trial meets the intent of the mechanism. The proposal body should address the review criteria as outlined in Section VI-B of this program announcement and should include the following seven parts:

Describe the proposed clinical trial using the outline provided below:

- State the objective and rationale of the proposed clinical trial, including any preclinical science and preliminary clinical research relevant to the trial;
- State the relevance of the proposed clinical trial to NF1, NF2, and/or Schwannomatosis;
- As appropriate, describe the proposed intervention(s) to be tested in the clinical trial, with a brief description of its source, IND status, availability of the substance in sufficient quantity under cGMP production, dosing, mechanism(s) of action, and preclinical/clinical efficacy;
- Provide a description of the patient population(s), an estimated sample size for the clinical trial, and a preliminary patient accrual/recruitment schedule;
- Outline the plan for the development of a clinical protocol and consent/assent form(s) and for obtaining both internal scientific and local IRB review at the highest possible level within each of the participating institutions, up to and including preliminary IRB approval if available at your institution(s), by the time of the Clinical Trial Award proposal submission;
- Describe the preliminary management plan for the clinical trial, including key participants and their contributions (additional information on collaborators can be included in the Biographical Sketch section, see item 9 below); and
- Provide some evidence that the institution will support the proposed clinical trial.

7. Abbreviations: Start section on a new page; one-page limit. Provide a list of all acronyms, abbreviations, and symbols used.

8. References: Start section on a new page; no page limit. List all relevant references using a standard reference format that includes the full citation (i.e., author(s), year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).

9. Biographical Sketches: Three-page limit per individual. Biographical sketches should be included for each of the key personnel listed on the budget page, including collaborating investigators and support staff. These documents are a critical component of the review process. Incomplete or missing biographical sketches may result in lower priority scores. The Biographical Sketch form may be used. Use of this form is not mandatory, but the information requested shall be presented in a similar format.

10. Existing/Pending Support: Start section on a new page; no page limit. List on a separate page the titles, time commitments, supporting agencies, durations, and levels of funding for all existing and pending research projects involving the PI and key personnel. If no support exists, state "none." Proposals submitted under this program announcement should not duplicate other funded research projects.

11. Facilities/Equipment Description: No page limit. Describe the facilities available for performance of the proposed research/services. Describe the institutional commitment, including any additional facilities or equipment proposed for purchase or available for use at no cost to the USAMRMC. Indicate if Government-owned facilities or equipment are proposed for use.

12. Questionnaires, Survey Instruments, or Clinical Protocols: No page limit. Include an appropriately titled page listing the documents you have included in this section.

13. Publications and/or Patent Abstracts: Five-document limit. Include up to five relevant publication reprints and/or patent abstracts. A patent abstract should provide a non-proprietary description of the patent application. If more than five such items are included in the submission, the extra items will not be peer reviewed.

14. Administrative Documentation: No page limit. Submit only material specifically requested or required in this program announcement. **This section is not for additional figures, tables, graphs, photographs, diagrams, chemical structures, pictures, pictorials, cartoons, or other relevant information needed to judge the proposal.** Unrequested material that is submitted may be construed as an attempt to gain a competitive advantage and will be removed; it may be grounds for administrative rejection of the proposal.

The first item in this section must be a list of all the items included in the Administrative Documentation section.

- Provide letter(s) of support from any collaborating individuals or institutions.
- Provide letter(s) of commitment from institutions that will be participating in the clinical trial.
- Provide documentation that the participating institutions have an intellectual property plan and are willing to resolve intellectual property issues.

All administrative documentation must be incorporated into the electronic PDF version of your proposal. Support documentation will not be accepted separately from the electronic proposal submission. All documents or letters requiring signatures must be signed and then incorporated into the submitted proposal.

F. Budget Information: Budget Information includes the Detailed Cost Estimate forms and Budget Justification. Budget Information is uploaded under the "Required Files" tab of the CDMRP eReceipt system.

1. Funding Restrictions: Funding for the Clinical Trial Development Award in FY04 is up to $150,000 per award inclusive of both direct and indirect costs for 18 months; funds will be disbursed in two installment payments, pending proposal, clinical protocol, and consent form submission. Funds from both installments of the Clinical Trial Development Award can cover administrative support including salary, meetings and related travel among participating investigators, database generation and software development, purchase of computers, design of websites, teleconferences, and other costs directly associated with planning and developing the clinical trial. Travel costs may not exceed $1,800 per year per investigator. *Funds may not be used to support laboratory research.*

Please note there is no guarantee that funds will be available for Clinical Trial Awards in FY05.

2. Detailed Cost Estimate Forms and Justifications Instructions: Budget is an important consideration in both peer and programmatic review, and applicants are cautioned to use discretion in budget requests. Budgets will also be reviewed during award negotiations. Complete justification must be provided for expenses in all categories. The Detailed Cost Estimate form and Justification for your proposal must be uploaded as a PDF file, separate from the proposal.

The following section provides instructions for preparing the Detailed Cost Estimate form. All amounts entered should be in U.S. dollars.

a. Personnel:

i. Name: Starting with the PI, list the names of all participants who will be involved in the project during the initial budget period, regardless of whether salaries are requested. Include all collaborating investigators, research associates, individuals in training, and support staff. Only **ONE** person may be identified as the PI of the proposal.

ii. Role on Project: Identify the role of each individual listed on the project. Describe his or her specific functions in the "Justification" section of the Detailed Cost Estimate form.

iii. Type of Appointment (Months): List the number of months per year reflected in an individual's contractual appointment with the applicant organization. The DOD staff assumes that appointments at the applicant organization are full time for each individual. If an appointment is less than full time, e.g., 50%, note this with an asterisk (*) and provide a full explanation in the "Justification" section of the Detailed Cost Estimate form. Individuals may have split appointments (e.g., for an academic period and a summer period). For each type of appointment, identify and enter the number of months on separate lines.

iv. Annual Base Salary: Enter the annual institutional base salary for each individual listed for the project.

v. Percentage of Effort on Project: The qualifications of the PI and the amount of time that he or she and other professional personnel will devote to the research are important factors in selecting research proposals for funding. For each key staff member identified on the budget form, list the percentage of each appointment to be spent on this project.

vi. Salaries Requested: Enter the salaries in whole dollar figures for each position for which funds are requested. The salary requested is calculated by multiplying an individual's institutional base salary by the percentage of effort on the project.

vii. Fringe Benefits: Fringe benefits may be requested in accordance with institutional guidelines for each position, provided the costs are treated consistently by the applicant organization for all sponsors. Documentation to support the fringe benefits should be provided.

viii. Totals: Calculate the totals for each position and enter these as subtotals in the columns indicated.

b. Consultant Costs: Regardless of whether funds are requested, provide the names and organizational affiliations of all consultants.

c. Major Equipment: It is the policy of the DOD that all commercial and non-profit recipients provide the equipment needed to support proposed research. In those rare cases where specific additional equipment is approved for commercial and non-profit organizations, such approved cost elements shall be separately negotiated. Moreover, it is expected that institutions will share 50% of the cost of equipment purchased for this research proposal when individual equipment costs are equal to or exceed $5,000.

d. Materials, Supplies, and Consumables: A general description and total estimated cost of expendable equipment and supplies are required. Itemize supplies in separate categories (e.g., glassware, chemicals, radioisotopes). Categories in amounts less than $1,000 do not need to be itemized. If animals are to be purchased, state the species, strain (if applicable), and the number to be used. If human cell lines are to be purchased, state the source and the description.

e. Travel Costs: Travel costs for scientific and technical meetings may not exceed $1,800 per year per investigator.

f. Research-Related Subject Costs: Itemize costs of subject participation in the research study. These costs are strictly limited to expenses specifically associated with the proposed study. The USAMRMC will not provide funds for ongoing medical care costs that are not related to a subject's participation in the research study.

g. Other Expenses: Itemize other anticipated direct costs such as publication and report costs, rental for computers and other equipment (provide hours and rates), and communication costs. Unusual or expensive items should be fully explained and justified. Estimate the costs of publishing and reporting research results, including direct charges for clerical preparation, illustrations, reprints, and distribution.

h. Subaward Costs: A description of services or materials that are to be awarded by subcontract or subgrant is required. For awards totaling $10,000 or more, provide the following specific information:

- Identification of the type of award to be used (e.g., cost reimbursement, fixed price);

- Identification of the proposed subcontractor or subgrantee, if known, and an explanation of why and how the subcontractor or subgrantee was selected or will be selected;
- Whether the award will be competitive and, if noncompetitive, rationale to justify the absence of competition; and
- The proposed acquisition price.

i. Indirect Costs (overhead, general and administrative, and other): The most recent rates, dates of negotiation, base(s), and periods to which the rates apply should be disclosed along with a statement identifying whether the proposed rates are provisional or fixed.

j. Total Costs for the Entire Proposed Period of Support (second page of the Detailed Cost Estimate form): Enter the totals under each budget category for all additional years of support requested and itemize these totals in the "Justification" section of the Detailed Cost Estimate form. Note with an asterisk (*) and explain any significant increases or decreases from the initial year budget. All amounts should be in U.S. dollars. Total costs for the entire proposed period of support should equal the amount previously entered online in the Proposal Information https://cdmrp.org/proposals.

3. Justification (third page of the Detailed Cost Estimate form): Each item in the budget should be clearly justified under the "Justification" section of the Detailed Cost Estimate form.

G. Regulatory Requirements: Completed and signed copies of the "Certificate of Environmental Compliance" and "Principal Investigator Safety Program Assurance Form" must be uploaded under the "Required Files" tab of the CDMRP eReceipt system as separate PDF files.

Do not submit other Regulatory Documents (Research Involving Human Subjects and/or Anatomical Substances; Research Involving Animals) with the proposal. Instead, the applicant should provide these documents to the USAMRMC only upon request.

H. USAMRAA Documents: The most current version of the institution's negotiated "Rate Agreement," the "Certifications and Assurances for Assistance Agreements," and the "Representations for Assistance Agreements" must be uploaded by the Contract Representative from the Sponsored Programs Office (or equivalent). These documents must be uploaded as separate PDF files under the Contract Representative's "My Profile" tab of the CDMRP eReceipt system prior to negotiations.

I. Submission Dates and Times: Proposals must be approved on the CDMRP eReceipt system by the Contract Representative at the applicant's institutional Sponsored Programs Office (or equivalent) by the deadline. If your proposal is either incomplete or not approved electronically before the deadline, it will not be considered for review. The eReceipt system will **not** accept data entry, file uploads, or approvals submitted after the 5:00 p.m. Eastern time May 4, 2004 deadline.

The timeline for Clinical Trial Development Awards is:

On-Line Letter of Intent:	As soon as possible but no later than April 6, 2004.
On-Line Proposal Information:	Prior to proposal submission.
Proposal Submission/Approval Deadline:	**5:00 p.m. Eastern time May 4, 2004.**
Proposal Review:	June 2004
Request for Additional Documents:	As early as 2 weeks after the completion of programmatic review.
Notification Letter:	Approximately 4 weeks after proposal review.
Award Start Date:	As early as August 2004.

J. Electronic Submission Requirements: Electronic submission is required. Proposals will be accepted only as PDF files submitted through the CDMRP eReceipt system at https://cdmrp.org/proposals.

Several steps are critical to successful proposal submission.

- The Proposal Information must be submitted prior to submission of the proposal. Applicants are encouraged to begin this part of the submission process early.
- The e-mail address of a Contract Representative from the Sponsored Programs Office (or equivalent) must be included.
- Applicants are encouraged to coordinate early with their Sponsored Programs Office.
- The Contract Representative from the Sponsored Programs Office (or equivalent) who is authorized to negotiate on behalf of the institution is required to provide final approval before the proposal is accepted.
- The eReceipt system will **not** accept data entry, file uploads, or approvals submitted after the 5:00 p.m. Eastern time May 4, 2004 deadline.
- Any supporting documentation that the applicant includes with the proposal must be incorporated into the PDF file prior to upload.
- Some items to be included in the proposal will need to be scanned. These items might include figures, tables, letters, or publications. All scanned documents, including figures, tables, and graphs, should be scanned at a resolution of 300-400 dpi or less.
- Budget Information includes the Detailed Cost Estimate form and the Budget Justification form. Budget Information must be uploaded under the "Required Files" tab of the CDMRP eReceipt system.
- The Regulatory documents required at submission include a completed, signed Certificate of Environmental Compliance and a completed, signed Principal Investigator Safety Program Assurance form. These must be uploaded under the "Required Files" tab of the CDMRP eReceipt system.

VI. PROPOSAL REVIEW INFORMATION

A. Proposal Review and Selection Overview: Clinical Trial Development Award proposals will be scientifically and programmatically reviewed by the NFRP Integration Panel (IP), which is composed of scientific experts, clinicians, and consumer advocates. The IP will determine which proposals best fulfill the intent of the award mechanism.

B. Review Criteria: Clinical Trial Development Award proposals will be evaluated according to the following criteria:

- **Clinical Relevance:** Does the applicant provide a clear scientific rationale for the proposed clinical trial? Do existing preclinical science and/or preliminary clinical research support the relevance of the clinical trial to NF1, NF2, and/or Schwannomatosis? Does the proposed clinical trial address an important problem related to the treatment of NF, and is it likely to have a substantial clinical impact?
- **Intervention:** Is the proposed intervention to be tested in the clinical trial adequately described and available? Is the intervention novel?
- **Clinical Trial:** Is the plan for the development of a clinical protocol within the time of the Clinical Trial Development Award appropriate? Is there a plan for obtaining both internal scientific review and local IRB approval(s) for the clinical protocol and consent form at the highest possible level within the institution, up to and including preliminary IRB approval, by the time of a Clinical Trial Award proposal submission? Are the preliminary sample sizes and patient accrual plans reasonable? Does the PI present evidence of access to an appropriate patient population? Is the outline of a clinical trial management plan present, and is it appropriate to the proposed clinical trial? Is a clear statistical plan, including sample size projections and power analysis, outlined in the proposal?
- **Principal Investigator and Personnel:** Does the PI have expertise in NF? Are the PI and other key personnel appropriately trained and well suited to carry out this work? Is there representation from all the areas of expertise needed to conduct the clinical trial successfully?
- **Institutional Commitment:** Is there evidence of institutional commitment to the proposed clinical trial at each participating institution? Is there evidence of an intellectual property management plan that is agreed upon by all participating institutions?

Scientifically sound proposals that best fulfill the above criteria and most effectively address the unique focus and goals of the program will be selected by the IP and recommended to the Commanding General, USAMRMC, for funding.

VII. AWARD ADMINISTRATION INFORMATION

A. Award Notices: After the evaluation process is completed, every applicant will receive notification of the award status of his or her proposal. Applicants can expect to be notified of the agency's decision in July 2004.

B. Administrative Requirements: All awards are made to organizations, not individuals. A PI should submit a proposal through, and be employed by or affiliated with, a university, college, non-profit research institute, commercial firm, or government agency (including military laboratories) in order to receive support. To be eligible for award, a prospective recipient should meet certain minimum standards pertaining to institutional support, financial resources, prior record of performance, integrity, organization, experience, operational controls, facilities, and conformance with safety and environmental statutes and regulations (Office of Management and Budget Circular A-110 and DOD Grant and Agreement Regulations). Any organization requesting receipt of an award from this announcement must be registered in the Central Contractor Registration (CCR) database. Access to the CCR online registration is through the CCR homepage at http://www.ccr.gov.

Any change in the institution, the PI, and/or the SOW will require that the PI resubmit contact information. Any delay in the submission of updated information could result in a delay in the contracting and regulatory review and a subsequent delay in payment.

C. Award Negotiation: Award negotiation consists of discussions, reviews, and justifications of critical issues involving USAMRAA. A Contract Specialist from USAMRAA will contact the Contract Representative from the Sponsored Programs Office (or equivalent) who is authorized to negotiate contracts and grants at the applicant's institution. As part of the negotiation process, additional documentation and justifications related to the proposed SOW and associated budgets may be required.

Note that the award start date will be determined during the negotiation process.

D. Regulatory Review:

1. Overview: Concurrent with the USAMRAA negotiations, the office of Surety, Safety and Environmental will review the Certificate of Environmental Compliance, and Principal Investigator Safety Program Assurance form submitted with the proposal. The USAMRMC RCQ office will review documents related to Research Involving Animal Use and Research Involving Human Subjects/Anatomical Substance Use submitted upon request to ensure that Army regulations are met.

2. Certificate of Environmental Compliance: The Certificate of Environmental Compliance must be submitted with the proposal. If multiple research sites/institutions are funded in your proposal, then a Certificate of Environmental Compliance for each site will be requested at a later date.

3. Safety Program Documents: The Principal Investigator Safety Program Assurance form must be submitted with the proposal.

A Facility Safety Plan is also required and will be requested at a later date. However, your institution may already have an approved Facility Safety Plan. To determine the status of approval, check the USAMRMC website at http://mrmc-www.army.mil/crprcqsohdfsplan.asp. If your institution is not listed on the aforementioned website, contact your Facility Safety Director/Manager to initiate completion of the institution-based Facility Safety Plan. Specific requirements for the Safety Program Plan can be found at http://mrmc-www.army.mil/docs/rcq/FY02FSPAppendix.doc.

If multiple research sites/institutions are funded in your proposal, then a Facility Safety Plan for each site/institution not listed in the aforementioned website will be requested at a later date.

4. Research Involving Animal Use: Animal use documents should not be submitted with the proposal and will be requested at a later date. Specific requirements for research involving animals can be found at http://mrmc-www.army.mil/docs/rcq/FY02AnimalAppendix.doc.

5. Research Involving Human Subjects/Anatomical Substances: Human Subjects and/or Anatomical Substances use documents should not be submitted with the proposal and will be requested at a later date. In addition to local Institutional Review Board (IRB) approval to conduct research involving human subjects and/or anatomical substances, a second tier of IRB review and approval is also required by the DOD. This second review is conducted by the Human Subjects Research Review Board (HSRRB), which is administered by the USAMRMC RCQ office. The HSRRB is mandated to comply with specific laws and directives governing all research involving human subjects that is conducted or supported by the DOD. These laws and directives are rigorous

and detailed and will require information in addition to that supplied to the local review board. For example:

- Intent to Benefit. In the development of a research protocol for submission to the DOD, the applicant must specifically address, if applicable, the Intent to Benefit. An individual not legally competent to consent (e.g., minors) may not be enrolled in DOD-sponsored research unless the research is intended to benefit each and every subject enrolled in the study. Applicants should be aware that this law makes placebo-controlled clinical trials problematic because of the 'intent to benefit' requirement whenever participation is sought of subjects from whom consent must be obtained by the legally authorized representative.
- The DOD considers cell lines of human origin to be human anatomical substances. Use of these cell lines is subject to HSRRB review and approval.

Specific requirements for research involving human subjects and/or anatomical substances can be found at http://mrmc-www.army.mil/docs/rcq/HSAppendix19Feb02.pdf. An informed consent form template can be located at http://mrmc-www.army.mil/docs/rcq/consentform_template.pdf.

6. Award/Regulatory Approval: Please note that each award mechanism has specific requirements regarding human subjects and animal use.

Once an award is made, the applicant may not use, employ, or subcontract for the use of any human subjects, human anatomical substances, or use of laboratory animals without express written approval from the applicable USAMRMC RCQ office. USAMRMC RCQ will forward these express written approvals directly to the applicant with a copy furnished to the institution's Sponsored Programs Office (or equivalent).

E. Reporting: All research awards will require the timely delivery of several reports during the research effort. Reporting requirements consist of an annual report (for each year of research except the final year) that presents a detailed summary of scientific issues and accomplishments and a final report (submitted in the last year of the award period) that details the findings and issues for the entire project.

VIII. OTHER INFORMATION

A. Disclosure of Proprietary Information outside the Government: By submission of a proposal, the applicant understands that proprietary information may be disclosed outside the Government for the sole purpose of technical evaluation. The USAMRMC will obtain a written agreement from the evaluator that proprietary information in the proposal will only be used for evaluation purposes and will not be further disclosed or utilized. Funded proposals may be subject to public release under the Freedom of Information Act; proposals that are not selected for funding will not be subject to public release.

B. Government Obligation: Applicants are cautioned that only an appointed Contracting/Grants Officer may obligate the Government to the expenditure of funds. No commitment on the part of the Government to fund preparation of a proposal or to support research should be inferred from discussions with a technical project officer. Applicants who, or organizations that, make financial or other commitments for a research effort in the absence of an actual legal obligation signed by the USAMRAA Contracting/Grants Officer do so at their own risk.

C. Information Service: Offerors may use the technical reference facilities of the National Technical Information Service, 5285 Port Royal Road, Springfield, Virginia, 22161, for the purpose of surveying

existing knowledge and avoiding needless duplication of scientific and engineering effort and the expenditure thereby represented. To the extent practical, all other sources should also be consulted for the same purpose.

D. Inquiry Review Panel: Applicants can submit a letter of inquiry to the USAMRMC in response to funding decisions made for a given proposal. Members of the CDMRP staff, USAMRMC Judge Advocate General staff, and USAMRAA Grants Officers constitute an Inquiry Review Panel and review each inquiry to determine whether factual or procedural errors in either peer or programmatic review have occurred, and if so, what action should be taken.

E. Title to Inventions and Patents: In accordance with the Bayh-Dole Act (35 USC 200 et seq.[2]), title to inventions and patents resulting from such federally funded research may be held by the grantee or its collaborator, but the U.S. Government shall, at a minimum, retain nonexclusive rights for the use of such inventions. An investigator must follow the instructions in the assistance agreement concerning license agreements and patents.

F. J-1 Visa Waiver: It is the responsibility of the awardee to ensure that the research staff is able to complete the work without intercession by the DOD for a J-1 Visa Waiver on behalf of a foreign national in the United States under a J-1 Visa.

[2]Title 35, United States Code, Section 200 et seq.

IX. ACRONYM LIST

AVI	Audio Video Interleave
CDMRP	Congressionally Directed Medical Research Programs
CFDA	Catalog of Federal Domestic Assistance
cGMP	Current Good Manufacturing Practice
CTDA	Clinical Trial Development Award
DOD	Department of Defense
FY	Fiscal Year
HBCU/MI	Historically Black Colleges and Universities/Minority Institutions
HSRRB	Human Subjects Research Review Board
IND	Investigational New Drug
IP	Integration Panel
IRB	Institutional Review Board
M	Million
MPEG	Moving Picture Experts Group
NF	Neurofibromatosis
NFRP	Neurofibromatosis Research Program
PDF	Portable Document Format
PI	Principal Investigator
RCQ	Regulatory Compliance and Quality
SOW	Statement of Work
USAMRAA	US Army Medical Research Acquisition Activity
USAMRMC	US Army Medical Research and Materiel Command
USC	United States Code
WAV	Wave